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13. ABSTRACT *(Maximum 200 words)*

BACKGROUND: This study compared the distribution of arterial oxygen saturation (SaO2) and susceptibility to Acute Mountain Sickness (AMS) in moderate altitude residents (MAR) and low altitude residents (LAR) following rapid ascent to 4,056 m. METHODS: Resting PETCO2 and SaO2 were measured in 38 subjects residing for > 3 months near Colorado Springs, CO (MAR group) at 1,940 m (USAF Academy) and after ~1hr at 4,056 m on the summit of Pikes Peak, CO following ascent by car. SaO2 was also measured at 610 m elevation intervals during the ascent. Thirty-nine LAR (50 m) group subjects were exposed to a similar ascent profile in a hypobaric chamber. RESULTS: At 1,940 m the MAR SaO2 and PETCO2 were 94 ± 1 %, ($\bar{X}$ S.D.) and 33.6 2.8 mmHg, respectively. At 3,048 m and higher, MAR SaO2 decreased reaching 86 2 % ($p < 0.001$) at 4,056 m, but PETCO2 (32.1 4.5 mmHg) was not affected. At 50 m the LAR SaO2 and PETCO2 were 98 1 % and 38.7 2.7 mmHg, respectively. At 1,940 m and higher, LAR SaO2 decreased ($p < 0.001$) reaching 82 5 % at 4,056 m, and PETCO2 (36.4 3.5 mmHg) decreased ($p < 0.05$). Above 2,438 m, the MAR SaO2 was higher ($p < 0.001$) than the LAR. Only 1 MAR subject, but 9 LAR subjects reported AMS symptoms. CONCLUSIONS: Ventilatory acclimatization developed during moderate altitude residence substantially enhances arterial oxygenation during rapid ascents to higher altitudes. Compared to prior studies, the level of ventilatory acclimatization achieved at moderate altitude is similar to residing at 4,056 m for approximately 5 - 9 days.

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Residence at Moderate Altitude Improves Ventilatory Response to High Altitude

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MUZA SR, ROCK PB, ZUPAN MF, MILLER JC, THOMAS WR, CYMERMAN A. *Residence at moderate altitude improves ventilatory response to high altitude.* Aviat Space Environ Med 2004; 75:1042–8.

Background: This study compared the distribution of arterial oxygen saturation (S_aO_2) and susceptibility to Acute Mountain Sickness (AMS) in moderate altitude residents (MAR) and low altitude residents (LAR) following rapid ascent to 4056 m. ***Methods:*** Resting $P_{ET}CO_2$ and S_aO_2 were measured in 38 subjects residing for > 3 mo near Colorado Springs, CO (MAR group), at 1940 m (USAF Academy), and after ~1 h at 4056 m on the summit of Pikes Peak, CO, following ascent by car. S_aO_2 was also measured at 610-m elevation intervals during the ascent. Of the LAR (50 m) group, 39 subjects were exposed to a similar ascent profile in a hypobaric chamber. ***Results:*** At 1940 m the MAR S_aO_2 and $P_{ET}CO_2$ were 94 ± 1% ($\bar{X}$ ± SD) and 33.6 ± 2.8 mmHg, respectively. At 3048 m and higher, MAR S_aO_2 decreased, reaching 86 ± 2% ($p < 0.001$) at 4056 m, and $P_{ET}CO_2$ (32.1 ± 4.5 mmHg) decreased ($p < 0.05$). At 50 m the LAR S_aO_2 and $P_{ET}CO_2$ were 98 ± 1% and 38.7 ± 2.7 mmHg, respectively. At 1940 m and higher, LAR S_aO_2 decreased ($p < 0.001$), reaching 82 ± 5% at 4056 m, and $P_{ET}CO_2$ (36.4 ± 3.5 mmHg) decreased ($p < 0.05$). Above 2438 m, the MAR S_aO_2 was higher ($p < 0.001$) than the LAR. Only one MAR subject, but nine LAR subjects reported AMS symptoms. ***Conclusions:*** Ventilatory acclimatization developed during moderate altitude residence substantially enhances arterial oxygenation during rapid ascents to higher altitudes. Compared with prior studies, the level of ventilatory acclimatization achieved at moderate altitude is similar to residing at 4056 m for approximately 5–9 d.

Keywords: hypoxia, arterial oxygen saturation, acute mountain sickness.

DURING LONG-TERM (days to weeks) exposures to high altitudes, humans compensate for the decreased inspired oxygen partial pressure (P_IO_2) by progressively increasing ventilation. For example, following rapid ascent to 4300 m elevation, ventilation increases during the first 6–8 d (13). The rise in ventilation produces a decrease in arterial carbon dioxide partial pressure (PCO_2) and a concomitant increase in P_aO_2 (21).

The time course and magnitude for acquiring ventilatory acclimatization has been well described for unacclimatized lowlanders rapidly ascending to high altitudes (> 3000 m). However, the magnitude of ventilatory acclimatization developed in lowlanders residing at moderate elevations (1000–2000 m) has not been well documented. Moreover, there is no comprehensive database that describes the degree to which ventilatory acclimatization to moderate altitudes improves arterial oxygenation on rapid ascent to altitudes above 2000 m. We propose that lowlanders acclimatized to moderate altitudes will maintain a higher level of arterial oxygenation when rapidly ascending to higher altitudes compared with lowlanders residing at low altitudes.

Numerous military installations housing large numbers of military personnel are located at moderate altitudes. Development of a database that describes the distribution of arterial oxygen saturation (S_aO_2) in lowlanders acclimatized to a range of moderate altitudes would provide commanders with ascent timetables to higher elevations that take full advantage of the personnel's acclimatization status. Furthermore, current limits on the time that aircrews of unpressurized aircraft may fly above 3048 m without supplemental oxygen are based on studies of unacclimatized lowlanders. Altitude-acclimatized aircrews may be able to safely operate beyond these limits, thus enhancing operational capability.

The purpose of this study was to determine the magnitude of ventilatory acclimatization in personnel acclimatized to moderate (1675–2255 m) altitude and the distribution of resting S_aO_2 following a rapid ascent and short stay at altitudes between 1940 and 4056 m. We tested the hypothesis that residents of moderate altitudes will maintain a higher level of arterial oxygenation when rapidly ascending to higher altitudes for a short duration compared with lowlanders residing at low altitudes. To determine if acclimatization to moderate altitude improves S_aO_2 at higher altitudes, comparisons were made between personnel acclimatized to moderate altitude and unacclimatized subjects residing near sea level.

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METHODS

The study protocol was approved in advance by Institutional Review Boards of the U.S. Army and U.S. Air Force. Each volunteer provided written informed consent before participating. Studies were conducted on 77 military personnel divided into two groups based on their residence altitude. The 38 moderate altitude residents (MAR) resided in the Colorado Springs, CO, metropolitan area (elevation ranging from 1675–2255 m). The MAR group consisted of 25 male and 13 female military personnel assigned to the U.S. Air Force Academy (USAFA) or Pederson AFB, CO. The 39 low altitude residents (LAR) resided near sea level (elevation 20–100 m) in the Boston, MA, metropolitan area. The LAR group volunteers were 30 male and 9 female military personnel assigned to SSCOM or ARIEM in Natick, MA. Personnel in each group had resided at their respective elevation for at least 3 mo prior to the study. All subjects regularly participated in aerobic physical conditioning and nearly half in strength conditioning. All the subjects had passed their most recent military physical performance test and were in good health. Female volunteers tested negative for pregnancy. The MAR group (34.8 ± 7.8 yr, range: 19–55 yr) was older ($p = 0.001$) than the LAR group (26.2 ± 8.8 yr, range: 18–45 yr), but otherwise were similar in height and weight.

The MAR group was studied first. For each subject, all testing was completed on 1 d. On the day of testing, subjects reported to an indoor test site located at the USAFA (Pb 606 ± 1 mmHg, pressure altitude 1940 m). At that site, several test procedures were performed: administration of an Environmental Background Survey (EBS) and the Environmental Symptoms Questionnaire (ESQ), and measurement of resting ventilatory parameters.

After completion of these procedures, subjects entered a van and were transported to the U.S. Army Pikes Peak Laboratory Facility on the summit (4300 m terrestrial elevation) of Pikes Peak, CO, via the Pikes Peak Highway. The van stopped at the following pressure altitudes according to the prevailing barometric pressure: 2438 m (Pb 560 ± 2 mmHg), 3048 m (Pb 521 ± 1 mmHg), 3658 m (Pb 484 ± 1 mmHg) and 4056 m (Pb 459 ± 1 mmHg). At each stop, the subjects remained in the van at rest for approximately 5 min, after which their S_{aO_2} and heart rate (HR) were recorded. On arriving at the summit, the same 5-min measurements were made, after which the subjects entered the U.S. Army Pikes Peak Laboratory Facility. The subjects' resting ventilatory parameters were measured within 50 min of arriving on the summit. After about 1 h on the summit, the subjects were administered the ESQ. The subjects then returned to the USAFA and were released from the study.

The LAR group was tested at the USARIEM hypobaric chamber facility, Natick, MA. The same test order and procedures previously performed on the MAR group were followed. Baseline measurements were made at the prevailing barometric pressure (759 ± 8 mmHg). Then the hypobaric chamber was decompressed at 305 $m \cdot min^{-1}$ to a pressure altitude of 1940 m (equivalent to the MAR baseline test altitude). After 20 min at this altitude, resting S_{aO_2} and HR were recorded. Then the same average ascent rate to higher altitudes previously obtained during the MAR group tests was duplicated in the hypobaric chamber. During all testing, the laboratory or vehicle ambient temperature was between 21–23°C.

At both test sites the following test procedures were performed. Each subject's height and weight were measured. Then each subject completed the EBS. The EBS is a 57-item questionnaire designed to elicit information on a test volunteer's previous experience in stressful climatic conditions, participation in physical activities, and medical history. The presence of hypoxic-induced symptoms (dizziness, shortness of breath, alertness, etc.) and the incidence of Acute Mountain Sickness (AMS) were determined from information gathered using the ESQ. The ESQ is a self-reported, 67-question inventory used to document symptoms induced by altitude and other stressful environments (17). A weighted average of scores from cerebral symptoms (headache, lightheaded, dizzy, etc.) designated AMS-C were calculated. AMS-C scores greater than 0.7 are defined as indicating the presence of AMS (17). Also, an alertness factor and fatigue factor were calculated from the questionnaire (17).

Each subject's resting minute ventilation (V_E), and end-tidal oxygen and carbon dioxide partial pressure (P_{ETO_2} and P_{ETCO_2}) were measured using an open-circuit metabolic measurement system (SensorMedics Vmax229,Viasys Healthcare, Yorba Linda, CA). Simultaneously, S_{aO_2} and HR were measured by pulse oximetry (N-200, Nellcor, Pleasanton, CA). The subjects were studied after having fasted for at least 2 h and having been seated at rest for at least 10 min. Resting ventilation was measured once at the subject's residence altitude (1940 m for the MAR group and 50 m for the LAR group), and once on arrival on the summit of Pikes Peak (MAR group) or the same equivalent pressure altitude in the hypobaric chamber (LAR group).

Statistical Analysis

To determine if acclimatization to moderate altitude improves arterial oxygen saturation at higher altitudes, two-way (residence altitude group and altitude exposure) analysis of variance with repeated measures in one factor (altitude exposure) was used to analyze the data. Data that deviated significantly from normality or failed to meet the qualifying assumptions of analysis of variance were analyzed using appropriate non-parametric techniques (i.e., ANOVA on ranks, or Mann-Whitney rank sum test). Possible gender influences were analyzed using the *t*-test, or if the data deviated significantly from normality or failed to meet the qualifying assumptions of analysis of variance, the data were analyzed using the Mann-Whitney Rank Sum Test. Lastly, potential relationships between measured parameters were tested using the Pearson Product Moment Correlation. Statistical significance was accepted at $p \leq 0.05$. All data are reported as the group mean ($\bar{X}$) ± SD.

TABLE I. RESTING VENTILATORY PARAMETERS AT RESIDENCE ALTITUDES AND FOLLOWING RAPID ASCENT TO HIGH ALTITUDES FOR THE LAR AND MAR SUBJECTS.

Group	Altitude (m)	$\dot{V}O_2$ ($L \cdot min^{-1}$)	$\dot{V}E$ ($L \cdot min^{-1}$)	$P_{ET}O_2$ (mmHg)	$P_{ET}CO_2$ (mmHg)	SaO_2 (%)	HR (bpm)
MAR	1940	0.30 ± 0.05	10.7 ± 2.3	75.4 ± 4.9	33.6 ± 2.8	94 ± 1	71 ± 11
	2438					94 ± 2	68 ± 9
	3048					92 ± 2†	68 ± 8
	3658					90 ± 2*†	68 ± 8*
	4056	0.28 ± 0.05	10.5 ± 2.6	51.5 ± 5.7†	32.1 ± 4.5*†	87 ± 3*†	68 ± 9*
LAR	50	0.22 ± 0.06	10.3 ± 1.8	105.9 ± 3.4	38.7 ± 2.7	98 ± 1	73 ± 10
	1940					96 ± 2†	70 ± 8
	2438					94 ± 2†	73 ± 10
	3048					91 ± 2†	75 ± 11
	3658					86 ± 3†	78 ± 12
	4056	0.25 ± 0.07	12.1 ± 2.5	48.0 ± 4.1†	36.4 ± 3.5†	82 ± 5†	83 ± 13†

$\bar{X}$ ± S.D. †$p < 0.05$ from Residence altitude; *$p < 0.05$ MAR vs. LAR.

RESULTS

MAR Group Results

Resting ventilatory parameters are listed in **Table I**. At the MAR test site, $P_{ET}O_2$, $P_{ET}CO_2$, and SaO_2 were significantly ($p < 0.05$) lower than normal values reported for lowlanders residing near sea level (6). During the approximately 2-h ascents to 4056 m, resting SaO_2 progressively decreased. The decrease in SaO_2 with increasing altitude was significant ($p < 0.001$) at and above the 3048-m elevation. There was no significant change in MAR resting HR during the ascent to 4056 m.

The SaO_2, $P_{ET}O_2$ and $P_{ET}CO_2$ decreased significantly between 1940 m and 4056 m in all MAR subjects (Table I), but there was no change in resting metabolic rate ($\dot{V}O_2$). The SaO_2 showed an 8% mean decrease between 1940 m and 4056 m. The range of SaO_2 at 4056 m was 83–93%. At 1940 m, effective alveolar ventilation (as assessed by $P_{ET}CO_2$) in the MAR group females was significantly greater than in the males (**Table II**), but there was no significant difference in these values between MAR group males and females at 4056 m. Interindividual differences in resting SaO_2 at 4056 m were not related to age, physical fitness, or frequency of trips to altitudes above 1940 m. For all MAR subjects, the $P_{ET}CO_2$ at their residence altitude (1940 m) showed a direct correlation to $P_{ET}CO_2$ ($r = 0.80$, $p < 0.0001$) at 4056 m and an indirect correlation to SaO_2 ($r = -0.42$, $p = 0.013$) at 4056 m. Likewise, the MAR subjects' resting SaO_2 at 2438 m and higher was positively correlated with their resting SaO_2 at each higher altitude (**Table III**).

Although there was a significant ($p < 0.001$) increase in AMS-C scores at 4056 m, only one MAR subject's AMS-C score met the diagnostic criterion for AMS. The mean AMS-C score (0.291 ± 0.194) at 4056 m was well below the 0.7 threshold criterion for AMS. Compared with 1940 m, fatigue scores showed a small but significant increase ($p < 0.001$) at 4056 m (0.165 ± 0.187 and 0.502 ± 0.378, respectively). The increase in fatigue scores was not correlated to any measured subject parameter. However, the alertness score was not affected by ascent to 4056 m.

LAR Group Results

At the LAR test site (50 m), resting SaO_2, $P_{ET}O_2$, and $P_{ET}CO_2$ were within the normal range for unacclimatized lowlanders (6). These values decreased significantly during ascent to 4056 m, but there was no change in resting metabolic rate. Specifically, the decrease in SaO_2 with increasing altitude was significant ($p < 0.001$) at and above 1940 m elevation (Table I). The SaO_2 showed a 16 ± 5% decrease between 50 m and 4056 m. The range of SaO_2 at 4056 m was 74–96%. At 50 m altitude, effective alveolar ventilation (as assessed by $P_{ET}CO_2$) in the LAR group females was significantly greater than in the males (Table II), but there was no significant difference between males' and females' SaO_2 at or above 1940 m, nor $P_{ET}CO_2$ or $P_{ET}O_2$ at 4056 m (Table II). Furthermore, interindividual differences in resting SaO_2 at 4056 m were not related to age, physical fitness, or frequency of trips to higher altitudes. For all LAR subjects, the $P_{ET}CO_2$ at their residence altitude (~50 m) showed a direct correlation to $P_{ET}CO_2$ at 4056 m (r =

TABLE II. BETWEEN-GENDER COMPARISON OF RESTING VENTILATORY PARAMETERS AT RESIDENCE ALTITUDES AND FOLLOWING RAPID ASCENT TO HIGH ALTITUDE FOR THE LAR AND MAR SUBJECTS.

		Men			Women		
Group	Altitude (m)	$P_{ET}CO_2$ (mmHg)	$P_{ET}O_2$ (mmHg)	SaO_2 (%)	$P_{ET}CO_2$ (mmHg)	$P_{ET}O_2$ (mmHg)	SaO_2 (%)
MAR	1940	34.2 ± 2.8	74.0 ± 4.9	94 ± 1	32.3 ± 2.1†	78.1 ± 3.7†	95 ± 1
	4056	32.7 ± 4.1	50.9 ± 4.5	86 ± 2	30.9 ± 5.0	52.8 ± 7.6	86 ± 3
LAR	50	39.3 ± 2.6	105.2 ± 3.4	98 ± 1	36.9 ± 2.2†	108.2 ± 2.1†	99 ± 1
	4056	36.6 ± 3.8	47.5 ± 4.1	82 ± 5	35.8 ± 2.4	49.8 ± 3.5	84 ± 6

$\bar{X}$ ± S.D. †$p < 0.05$ women vs. men within MAR and LAR groups.

TABLE III. CORRELATION COEFFICIENTS (R) BETWEEN RESTING SAO_2 AT 2438 M AND HIGHER ALTITUDES FOR THE LAR AND MAR SUBJECTS.

Group	Altitude	3048 m	3658 m	4056 m
MAR	2438m	0.65*	0.40*	0.30
	3048m	—	0.56*	0.51*
	3658m		—	0.78*
LAR	2438m	0.50*	0.58*	0.36*
	3048m	—	0.63*	0.64*
	3658m		—	0.54*

*$p < 0.05$

0.56, $p = 0.0002$) and an indirect correlation to $P_{ET}O_2$ ($r = -0.40$, $p = 0.011$), but not S_aO_2 at 4056 m. Likewise, the LAR subjects' resting S_aO_2 at 2438 m was positively correlated with their resting S_aO_2 at each higher altitude (Table III).

In the LAR group, there was a significant ($p < 0.001$) increase in AMS-C scores at 4056 m (0.360 ± 0.363). Although the mean AMS-C score was well below the 0.7 threshold criterion for AMS, the AMS-C scores of nine subjects in the LAR group met the criteria for diagnosis of AMS. There was no correlation between AMS symptom scores and resting ventilation parameters at 4056 m, or age and gender. Compared with 50 m, fatigue scores showed a small but significant ($p < 0.05$) increase at 4056 m (0.215 ± 0.222 and 0.703 ± 0.489, respectively). However, alertness was not affected by ascent to 4056 m.

MAR and LAR Comparison

At 1940 m the MAR group's $P_{ET}O_2$, $P_{ET}CO_2$, and S_aO_2 were lower ($p < 0.001$) than the sea level values obtained from the LAR subjects (Table II). After the LAR subjects were decompressed to 1940 m in the hypobaric chamber, their S_aO_2 values were not significantly different from the MAR group at that altitude (Table I) or at 2438 m. However, with further ascent above 2438 m, the MAR group's resting S_aO_2 was significantly greater than the LAR group's resting S_aO_2 at all higher altitudes. Ultimately, the mean difference in S_aO_2 between the two groups increased to 5% with ascent to 4056 m. The distribution of resting S_aO_2 for both groups at altitudes between 1940 to 4056 m is illustrated in **Fig. 1.** In addition to the shift to lower resting S_aO_2 in both groups with increasing altitude, these frequency distribution histograms clearly show that the range of resting S_aO_2 widened more in the LAR group than in the MAR group at all altitudes.

At 4056 m, the greater ventilation in the MAR group compared with the LAR group is substantiated by the MAR group's higher $P_{ET}O_2$ and lower $P_{ET}CO_2$ (Table I). This shift to a lower resting $P_{ET}CO_2$ in the MAR group relative to the LAR group is also present at their respective residence altitudes (Table I). When the two groups' resting $P_{ET}CO_2$ values were combined, the wide range of individual resting $P_{ET}CO_2$ values yielded a significant direct correlation between residence altitude $P_{ET}CO_2$ and their $P_{ET}CO_2$ at 4056 m and an indirect correlation to S_aO_2 at 4056 m (**Fig. 2**).

The mean AMS-C scores at 4056 m were not significantly different between the MAR and LAR groups. However, as noted earlier, nine LAR subjects but only one MAR subject had symptom scores consistent with the presence of AMS. Fatigue scores between the two groups showed a significant ($p = 0.049$) difference, with the MAR group having a lower fatigue score. There was no difference in alertness scores between the two groups.

DISCUSSION

The key findings from this study are as follows: 1) MAR residing at ~2000 m for greater than 90 d are mildly hypoxic at their residence altitude; 2) above 2438 m, the MAR group's resting S_aO_2 was higher than the LAR group's; 3) with increasing altitude, the range of resting S_aO_2 widened more in the LAR group than in the MAR group; 4) for all subjects, the $P_{ET}CO_2$ at their residence altitudes showed an indirect correlation to

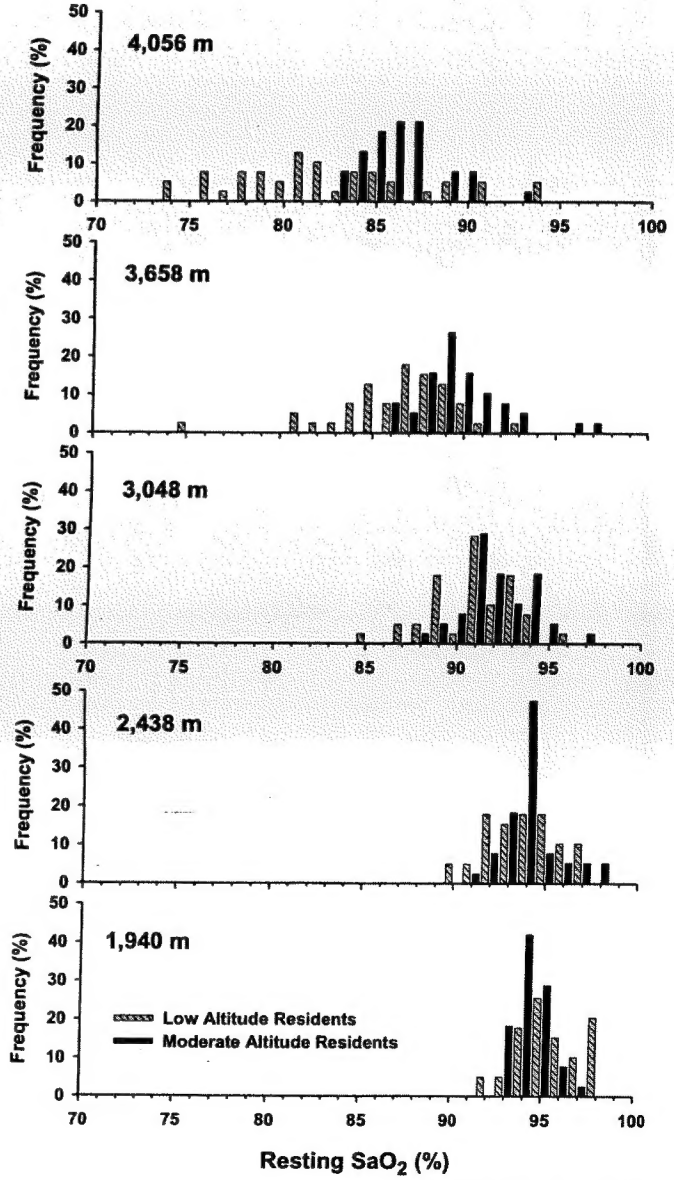

Fig. 1. Frequency distribution histograms of resting S_aO_2 for both MAR and LAR groups at altitudes between 1940 to 4056 m.

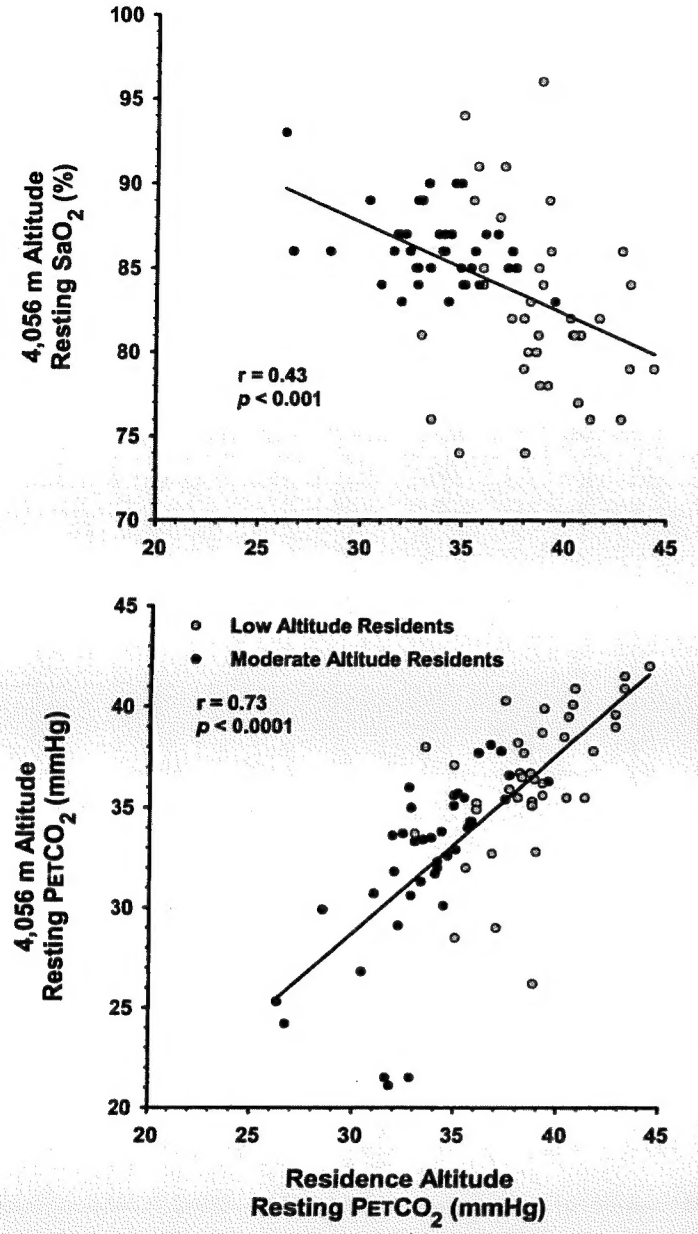

Fig. 2. Correlations between residence altitude resting $P_{ET}CO_2$ and resting $P_{ET}CO_2$ and SaO_2 at 4056 m for all subjects (MAR and LAR groups combined).

$P_{ET}O_2$ and a direct correlation to $P_{ET}CO_2$ at 4056 m; and 5) only one of the MAR subjects but nine of the LAR subjects developed AMS during this brief ascent to 4056 m. These findings are consistent with our hypothesis that lowlanders acclimatized to moderate altitudes will maintain a higher level of arterial oxygenation when rapidly ascending to higher altitudes compared with lowlanders residing at low altitudes.

This study was designed to make a direct comparison of ventilatory and symptom responses to high altitude between MAR and LAR groups. Ideally, the study design would have used one military population initially residing at low altitude, which was then translocated to moderate altitude. Such a design would control for possible individual subject characteristics that may modify ventilatory and symptom responses to high altitude. This ideal design was not feasible given the requirement for long-term residence at a moderate altitude. Overall, our two populations were remarkably similar, the only exception being the older age of the MAR subjects. However, we found no relationship between age and any of the outcome measurements that we made. Based on published SaO_2 values at 4056 m in LAR (12,13), we calculated that for a between groups comparison a sample size of approximately 40 subjects per group should yield a 99% C.I. with a 4% SaO_2 range. This SaO_2 range was selected because it is equal to the measurement error of many pulse oximeters, including the type used in this study. Post hoc, the SaO_2 99% C.I. was 1% and 2% for the MAR and LAR groups, respectively. Thus, there is a 99% probability that our results are representative of the population true mean, and well within the measurement error of pulse oximeters. Since all MAR and LAR subjects met their respective services fitness and medical retention standards, we believe that our results are applicable to any military population residing at similar elevations for comparable durations. Lastly, although the MAR subjects' ascent in a car had different environmental stimuli (visual and auditory) than the chamber ascent, we conclude the transportation mode had no effect on our measurements given that the vehicle had been stopped for at least 5 min, subjects had been quietly seated, and there was no elevation of heart rate in the car relative to the USAFA baseline studies (Table I).

On one hand it is not a remarkable finding that individuals acclimatized to moderate high altitude (~2,000 m in this study) sustained a higher level of ventilation than unacclimatized lowlanders. However, this study provides the first quantitative assessment of the degree of ventilatory acclimatization achieved by a fit population residing at moderate altitudes. Thus, this work provides a quantitative basis for developing models and establishing guidelines for protecting unit health and sustaining operational performance during operations in high mountainous terrains

Given the relatively large sample size used in this study, analysis of the dispersion of the ventilatory parameters measured was possible. The most significant finding was that the unacclimatized LAR subjects demonstrated a wider range of ventilatory responses to increasing high altitudes relative to the acclimatized MAR subjects (Fig. 1). This suggests that altitude acclimatization narrows the interindividual differences within a given population. Review of ventilatory data published from previous studies (12,13) of lowlanders residing for 12 or more days at 4056 m demonstrate a similar narrowing of the range of ventilatory responses as acclimatization develops. We suspect that this narrowing of interindividual differences is primarily achieved by raising the ventilatory responses of subjects that initially demonstrate the lowest ventilatory response to acute hypoxia (Fig. 1). The present study suggests that the level of ventilatory acclimatization achieved at moderate altitude was sufficient to narrow the interindividual ventilatory differences at higher altitudes. Thus, moderate altitude residence results in a

more uniform level of ventilatory acclimatization within that population.

As noted, previous studies have reported a large variation among individuals in the degree of ventilatory acclimatization at high altitude (18,20). Reeves et al. (13) reported that the variability in the degree of ventilatory acclimatization at high altitude was related to the individual's sea level end-tidal P_{ETCO_2}. That is, the lower the individual's P_{ETCO_2} at sea level, the greater their ventilation at high altitude. The current study extends this relationship to subjects residing at moderate altitude (Fig. 2). This relationship may be potentially useful in predicting an individual's ventilatory response and subsequent well-being to a future high-altitude exposure. However, measurement of P_{ETCO_2} requires sensitive analyzers and respiratory measurement apparatus that do not lend themselves to widespread use. Conversely, measurement of S_{aO_2} by pulse oximetry is technically easy and commonly used at high altitudes. But at low altitudes S_{aO_2} cannot provide a measure of individual ventilatory acclimatization status because of the relatively flat shape of the oxyhemoglobin disassociation curve above 70 mmHg arterial P_{O_2} (9). At high altitudes, as the arterial P_{O_2} drops, the curve is steeper and the measured S_{aO_2} can provide an assessment of ventilatory acclimatization status. In the present study, measurement of resting S_{aO_2} at altitudes of 2438 m or more (Table III) were predictive of resting S_{aO_2} at higher altitudes. This finding suggests that measurement of S_{aO_2} at or above 2438 m altitude can be a useful clinical tool for assessing ventilatory acclimatization status and identifying individuals more inclined to develop a relatively greater degree of hypoxemia on further ascent.

Another factor that may contribute to interindividual variation of responses to high altitude is gender. Although this study was not designed to compare ventilatory and symptom responses at high altitudes between men and women, the number of female subjects tested was large enough to provide an opportunity for comparison. As shown in Table II, at their respective residence altitudes, women had higher levels of ventilation relative to their metabolic rate than men, but at higher elevations no significant differences between genders were observed. These observations are consistent with our previous findings at high altitude (12).

This study did not provide a comparison between the MAR group and a LAR group that had achieved full ventilatory acclimatization to 4056 m by residing at that altitude. However, numerous studies have reported the ventilatory response on arrival and during residence at 4056 m on the summit of Pikes Peak (3,4,12,13,22). The results of two of these studies (12,13) and our current study are illustrated in **Fig. 3**. When sea level residents rapidly ascend to a pressure altitude of 4056 m, on arrival their P_{ETCO_2} is 34.9 ± 2.8 mmHg and their S_{aO_2} is 81 ± 5%. It takes 9–12 d of continuous residence at high altitude for the S_{aO_2} to rise to 88 ± 2%. By comparison, on rapid ascent to 4056 m, the MAR subjects' resting S_{aO_2} was 86 ± 2%. These data suggest that personnel residing at ~2000 m elevation for more than 90 d have

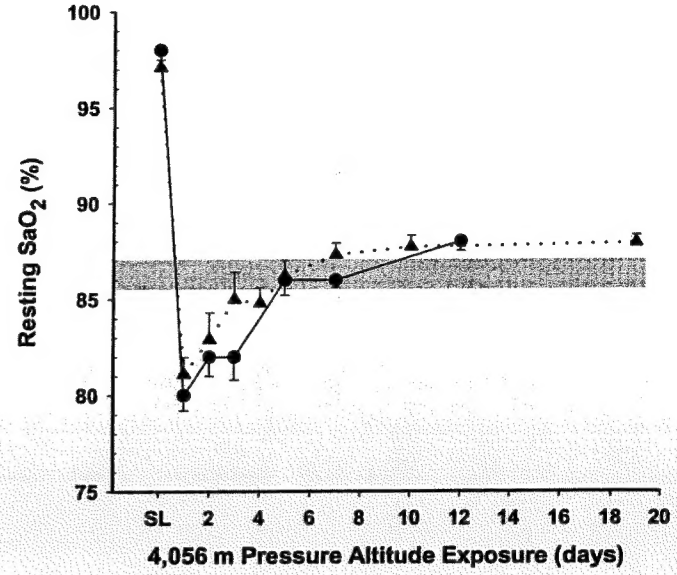

Fig. 3. Comparison of MAR groups' resting S_{aO_2} ($\bar{X}$ ± 95% confidence interval) to LAR subjects from two prior ventilatory acclimatization studies at 4056 m. Filled circles = lowlander women (12); filled triangles = lowlander men (13); and shaded bar = moderate altitude residents (95% CI).

acquired a level of ventilatory acclimatization equivalent to residing at 4056 m for 5–9 d.

In many individuals, the stress of the hypoxic environment causes physiological dysfunctions, which may be manifest in the form of several altitude illnesses including AMS. AMS is a syndrome that is characterized by headache, anorexia, nausea, vomiting, insomnia, lassitude, and malaise (14). The syndrome has great individual variation in susceptibility; however, the hypoxia-induced symptoms are most common in unacclimatized, low-altitude residents who rapidly ascend to terrestrial elevations exceeding 2500 m. The symptoms of AMS commonly appear within 4 to 24 h of exposure, and usually resolve after several days as acclimatization to hypoxia is achieved.

There is evidence that AMS-susceptible subjects have a relatively greater degree of hypoxemia compared with well subjects at high altitude. Many studies have reported that compared with well subjects, subjects who will develop and who have developed AMS have either a lower alveolar ventilation, alveolar oxygen partial pressure (P_{AO_2}) or S_{aO_2}, or higher alveolar carbon dioxide partial pressure (P_{ACO_2}) (1,5,7,10,11,15,19). Although two recent studies (8,16) did not find significant differences in ventilation or S_{aO_2} between sick and well subjects at high altitude, the balance of data suggests a relatively greater hypoxemia in AMS-susceptible subjects compared with non-susceptible subjects at high altitude.

Given the degree of ventilatory acclimatization achieved by the MAR group, we would expect such personnel to be less susceptible to AMS. Our results are consistent with this view. Only one subject in the MAR group developed AMS, whereas nine subjects in the LAR group did. Although the low incidence of AMS in the MAR group was predicted, because of the short exposure duration we cannot discount the possibility

that more members of the MAR group might have developed AMS had the exposure duration been longer.

In summary, the results of this study support our hypothesis that lowlanders acclimatized to moderate altitudes will maintain a higher level of arterial oxygenation when rapidly ascending to higher altitudes compared with lowlanders residing at low altitudes. These data suggest that personnel residing at ~2000 m elevation for more than 90 d have acquired a level of ventilatory acclimatization similar to residing at 4056 m for 5–9 d. The results also suggest that measurement of resting S_aO_2 at altitudes of 2438 m or more are predictive of resting S_aO_2 at higher altitudes and may be a useful clinical tool for assessing ventilatory acclimatization in a field or operational setting.

Finally, we speculate that given the degree of ventilatory acclimatization achieved by personnel residing at the moderate altitude studied, we would expect such personnel to be less susceptible to high altitude sickness and decrements in cognitive and physical performance during rapid ascent to higher altitudes. Lowlanders who have achieved the level of acclimatization seen in our MAR group usually have complete restoration of cognitive performance and substantial improvements in physical work performance (2,23). However, quantitative assessment of the effects of moderate altitude residence on cognitive and physical work performance will require further studies. Nevertheless, the results of the present study suggest that military personnel residing at moderate altitudes for a period of at least 90 d can be rapidly deployed to higher altitudes of up to 4056 m with a low probability of developing AMS and experiencing significant performance decrements.

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